A monthly update of PLRC happenings



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- Welcome to Dr. Irina Bochkis

#### Upcoming Seminars & Meetings

- Jan 29th @ 12PM Dr. Jingxing Ou, S120 BST
- Jan 30th @ 12PM Dr. Robert Schwartz, S120 BST
- Feb 13th @ 12PM Dr. Pam Hoodless, S120 BST
- Funding Opportunities
- Announcements & Meetings
  - UPMC Med Hepatology Annual Update 2/3/24
  - PLRC EAB Meeting 2/6/24
  - Hepatic Sinusoid Meeting 4/24-26/2024
  - ASIP/SLAM Meeting 6/16-20/2024

#### • Want Ads :

- Open positions
- Jobseekers CVs posted

Please acknowledge <u>all support</u> from the PLRC in your publications and presentations. Note the grant number and all CORES used. (NIH/NIDDK P30DK120531)

Please share your relevant accolades (grants, publications, awards and other news worthy items) with us, as it relates to the PLRC mission, so we can share with all of our members.

Visit the PLRC website (<u>www.livercenter.pitt.edu</u>) for up-to-date news, seminar and event information. Contact Aaron Bell (<u>bellaaro@pitt.edu</u>) if you have specific questions or suggestions.

#### Our mailing address is:

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### **FACULTY HIGHLIGHT**



GSBC Core directors Silvia Liu and Jianhua Luo along with Alina Ostrowska and Alex Soto-Gutierrez of the HSLBC published an article in eLife entitled, "Long-read single-cell sequencing reveals expressions of hypermutation clusters of isoforms in human liver cancer cells".

Silvia Liu, Yan-Ping Yu, Bao-Guo Ren, Tuval Ben-Yehezkel, Caroline Obert, Mat Smith, Wenjia Wang, Alina Ostrowska, Alejandro Soto-Gutierrez, Jian-Hua Luo (2024) Long-read single-cell sequencing reveals expressions of hypermutation clusters of isoforms in human liver cancer cells eLife 12:RP87607: <u>https://</u> doi.org/10.7554/eLife.87607.3

#### **ABSTRACT:**

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The protein diversity of mammalian cells is determined by arrays of isoforms from genes. Genetic mutation is essential in species evolution and cancer development. Accurate long-read transcriptome sequencing at singlecell level is required to decipher the spectrum of protein expressions in mammalian organisms. In this report, we developed a synthetic long-read single-cell sequencing technology based on LOOPSeq technique. We applied this technology to analyze 447 transcriptomes of hepatocellular carcinoma (HCC) and benign liver from an individual. Through Uniform Manifold Approximation and Projection analysis, we identified a panel of mutation mRNA isoforms highly specific to HCC cells. The evolution pathways that led to the hyper-mutation clusters in single human leukocyte antigen molecules were identified. Novel fusion transcripts were detected. The combination of gene expressions, fusion gene transcripts, and mutation gene expressions significantly improved the classification of liver cancer cells versus benign hepatocytes. In conclusion, LOOPSeq single-cell technology may hold promise to provide a new level of precision analysis on the mammalian transcriptome.



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#### FACULTY HIGHLIGHT

Dr. Yu-Chiao (Chris) Chiu, Assistant Professor of Medicine in the Hematology/Oncology department at Hillman cancer center published a paper in a Cell Press journal "Patterns" entitled, "shinyDeepDR: A user-friendly R Shiny app for predicting anti-cancer drug response using deep learning". Dr. Paul Monga was a coauthor on the article and Dr Chiu is a PLRC P&F grant recipient.

- shinyDeepDR is a web tool for predicting responses to 265 anti-cancer compounds
- It is applicable for researching both cancer cell lines and tumors
- Its interactive web interface facilitates result interpretation and investigation
- It identifies promising targets for an "undruggable" mutation in liver cancer

#### The Web tool is available online at: https://shiny.crc.pitt.edu/shinydeepdr/

Li-Ju Wang, Michael Ning, Tapsya Nayak, Michael J. Kasper, Satdarshan P. Monga, Yufei Huang, Yidong Chen, Yu-Chiao Chiu, shinyDeepDR: Patterns, 2024, 100894,ISSN 2666 3899, https://doi.org/10.1016/j.patter.2023.100894.

#### The bigger picture:

Understanding how different genomic attributes affect drug responses in cancer is crucial for personalized oncology. Deep learning, an advanced computational method, has demonstrated significant potential in identifying and predicting these intricate interactions. One such example is the DeepDR model, which predicts how cancer cells respond to drugs. However, not all researchers have the computational resources and programming expertise to leverage this potential. Here, we introduce shinyDeepDR to bridge this gap by providing an intuitive and user-friendly web platform to access DeepDR. In the broader scope, we envision that tools like shinyDeepDR will advance cancer research by making sophisticated computational models more FAIR (findable, accessible, interoperable, and reusable).

Advancing precision oncology requires accurate prediction of treatment response and accessible prediction models. To this end, we present shinyDeepDR, a user-friendly implementation of our innovative deep learning model, DeepDR, for predicting anti-cancer drug sensitivity. The web tool makes DeepDR more accessible to researchers without extensive programming experience. Using shinyDeepDR, users can upload mutation and/or gene expression data from a cancer sample (cell line or tumor) and perform two main functions: "Find Drug," which predicts the sample's response to 265 approved and investigational anticancer compounds, and "Find Sample," which searches for cell lines in the Cancer Cell Line Encyclopedia (CCLE) and tumors in The Cancer Genome Atlas (TCGA) with genomics profiles similar to those of the query sample to study potential effective treatments. shinyDeepDR provides an interactive interface to interpret prediction results and to investigate individual compounds. In conclusion, shinyDeepDR is an intuitive and free-to-use web tool for in silico anti-cancer drug screening.

#### YOUNG INVESTIGATOR HIGHLIGHT

Anu Balogun, MS., postdoctoral trainee in Dr Kari Nejak-Bowen's lab, will be giving the ASIP Young Investigator Keynote Seminar virtually on February 15th @ 1:00PM. The title of





Anu R. Balogun, MS, PhD Candidate University of Pittsburgh Pittsburgh, PA

ASIP

her talk is: "New Insights into Autophagy in Porphyria". Register online @ ASIP-Keynote



## PLRC SEMINARS

Jan 29th @ 12:00 pm – 1:00 pm in S120 BST

HSLBC \*\*Special Seminar\*\*



#### Jingxing Ou, PhD

Professor The 3rd Affiliated Hospital,

Sun Yat-sen University, China

Seminar Title: Hibernation-inspired mechanisms in promoting liver protection and regeneration.

#### Jan 30th @ 12:00 pm - 1:00 pm in S120 BST



Robert Schwartz, MD, PhD Associate Professor of Medicine,

Physiology, Biophysics, Systems Biology, & Biomedical Engineering

Cornell University, NY

Seminar Title: Leveraging Bioengineered and Primary Tissues to Study Human Liver Diseases

#### Feb 13th @ 12:00 pm – 1:00 pm in S120 BST



#### Pamela Hoodless, PhD

Professor, Medical Genetics and Biomedical Engineering Director, BCCRI Integrated Mouse Modelling Services (IMMS), Associate Member, Bioinformatics Training Program, CIHR University of British Columbia Vancouver, BC

Seminar Title: Transcriptional and Epigenetic Dynamics during Hepatic Specification

#### **NOTICE!**

NIH GRANT SUBMISSION DEADLINES ARE <u>NOT AFFECTED</u> BY GOVERNMENT SHUTDOWN AS OF NOW. Please submit by the standard dates

## **FUNDING OPPORTUNITIES**

Notice of Participation of NIDDK in PAR-23-309 Health and Health Care Disparities Among Persons Living with Disabilities (R01 - Clinical Trials Optional) (NOT-DK-24-006) National Institute of Diabetes and Digestive and Kidney Diseases

#### NOFOs:

<u>RFA-DK-25-003</u> Silvio O. Conte Digestive Diseases Research Core Centers (P30 Clinical Trial Optional) Plan for Enhancing Diverse Perspectives (PEDP), DMS. Etc changes in effect January 2024

Stephen I. Katz Early Stage Investigator Research Project Grant <u>PAR-24-075</u> (innovative project that represents a change in research direction for an early stage investigator (ESI) and for which no preliminary data exist) 1/26 or 5/29 due dates

#### Diabetes: JDRF Grant Opportunities <u>URL/LINK</u>

Improving Predictability of Food-Drug and Drug-Drug Interaction Risks by Utilizing In Vitro Simulated Gastrointestinal Dissolution Model for High-Risk Oral Drug Products (U01) Clinical Trial Optional <u>RFA-FD-24-009</u> <u>Open: 1/15/24 LOI 2/15/24</u>

To see all NIH Grants sorted by week, please visit: NIH Guide: 2023

Or click below for recent weeks:

Week of: <u>Jan 5:</u> <u>Jan 12:</u> <u>Jan 19:</u> <u>Click here</u> for all current <u>NIDDK</u> Funding opportunities



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### FACULTY HIGHLIGHT

The PLRC Administration would like to extent a warm welcome to our newest Full member, Associate Professor of Pathology, Dr. Irina Bochkis, PhD. Irina comes to us from the University of Virginia, and she has established a R01-funded research program studying genetic an epigenetic mechanisms regulating liver metabolism. Her lab focuses on genome-wide chromatin changes underlying physiological dysfunction, which include chromatin accessibility, nuclear localization & dynamics,

and genome organization. Our laboratory utilizes functional genomics, chromatin biology, physiology, and transcriptional regulation in a comprehensive approach to decipher molecular mechanisms in mammalian models of human metabolic disease (diabetes and diabetes-related metabolic dysfunction-associated steatotic liver disease, MASLD). WELCOME ABOARD!

## **ANNOUNCEMENTS & Meetings**

<u>Communityliveralliance.org</u>





 5<sup>th</sup> Annual UPMC Annual Update in Medical Hepatology (2024) @ The University Club, Pitt Campus. February 3, 2024 8:00AM-3:00PM In-person or Virtual option <u>Agenda</u>: <u>Registration</u>

All trainees and medical students are invited, and attendance is encouraged for those interested in GI and liver subspecialties. Registration is FREE for trainees and nurses/APPs thru Monday Jan. 22<sup>nd</sup>.Questions? Contact Joy@ <u>JOJ2@PITT.EDU</u>

- PLRC External Advisory Board Meeting @ 1104 Scaife Hall Conference Center 2/6/24 9AM-4PM
- ASIP Annual Meeting "Pathobiology: Mechanisms of Disease 2024": Baltimore, MD: April 20-23, 2024: <u>Registration:</u> event <u>Program</u>
- THE LIVER SINUSOID MEETING @ Chicago, IL April 24-26, 2024 Program: Registration
- Digestive Disease Week 2024: Washington D.C May 18-21, 2024
  <u>Registration</u>: Details
- The FASEB Liver Meeting is now the Summer Liver Academy Meeting (SLAM).@ Cape Coral, FL June 16-20, 2024 <u>Website</u>



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## WANT ADS

This section is available for PLRC members to communicate wants or needs in your laboratories. Available positions / Collaboration ideas / Equipment needs

Please send any "wants/needs" to be advertised to Aaron Bell (bellaaro@pitt.edu)

## **OPEN POSITIONS:**

### **JOB SEEKERS:**

- \* PhD, Senior Researcher at Hormel Institute, interested in Senior Lab role @ Pitt/UPMC. Experience with HCC, CCA, Mol. Biology, metabolism, signal transduction. Link to CV Email: kpant@umn.edu
- \* MD, PhD Researcher with extensive experience in cholangiocyte biology, strong PI references. Link to CV. Email: Qin.Li7@chp.edu
- \* Res.Asst.Prof. Highly experienced researcher in many disciplines including bioinformatics, proteomics, genomics and molecular biology. <u>Link to CV</u> Email: liz45@pitt.edu
- \* Sr. Postdoc from UPENN (Wells-Lab), Hepatobiliary toxicity, environmental toxins, organ-on-achip, mechanobiology and biomaterials. <u>Link to CV</u> Email: Kapish.Gupta@Pennmedicine.upenn.edu
- \* Postdoc/Research Associate from Wash U with experience in Immunology & cytokine signaling of liver diseases and liver regeneration. Interest in gene editing research. <u>Link to CV</u> Email: <u>ramavathnareshnaik@gmail.com</u>